



Advancing the art of tuberculosis detection

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ALAMOS, N.M., April 19, 2013—New work from Los Alamos National Laboratory shows promise for stemming the advance of tuberculosis (TB) by revealing how the bacterium interacts with its human hosts and thus providing a new pathway for early detection in patients.

A recent publication from the Los Alamos Biosensor Team describes the association of a key tuberculosis virulence factor, lipoarabinomannan (LAM) with human high-density lipoproteins (HDL) in blood. “Understanding the pathophysiology of tuberculosis, and the distribution of pathogen-associated molecules in the host, is essential to developing efficient methods of intervention,” said Harshini Mukundan, corresponding author on the paper.

“Association of lipoarabinomannan with high density lipoprotein in blood: Implications for diagnostics” *Tuberculosis* 93 (2013) was published April 3rd, 2013, in the journal *Tuberculosis*.

The team’s efforts have focused on using the LAM virulence factor as a sensitive indicator for TB. The problem has been that the biomarker, while being a reliable early indicator of TB, is very difficult to detect, especially in blood. Previously, the team has developed strategies for the detection of this biomarker in urine (Mukundan H et al, *Tuberculosis*, June 2012). Subsequently, they developed a strategy for the ultra-sensitive detection of the biomarker using a novel method, called membrane insertion (Mukundan H et al, *Tuberculosis*, Jan 2012)

The researchers extend the membrane insertion approach to the detection of molecules like LAM in patient serum using a device called an ultrasensitive wave-guide based biosensor. The measurement technique, or assay, exploits both the water-repellant and absorbent properties of LAM, a feature common to many bacterial virulence factors. These measurements raised a key question as to why the quantities of LAM in blood serum are usually low, despite high concentrations in urine from the same individuals. It appears that LAM, an amphiphile (meaning it has both hydrophobic and hydrophilic components), is associated with carrier molecules such as HDL (a lipoprotein) in the blood of patients infected with tuberculosis. The concept is very simple. A drop of oil will not be free-floating in water. Similarly, amphiphilic LAM cannot be free floating in aqueous blood, but it associates with carrier molecules such as the lipoprotein HDL. Such an association is likely to affect host–pathogen interactions, pathogen distribution and clearance in the host, and must be thoroughly understood for the effective design of vaccines and diagnostics. The team has exploited this interaction to design a novel assay for the capture of such molecular components, termed HDL capture.

As it happens, many bacterial virulence factors share similar biochemical properties as LAM. Examples include the lipopolysaccharide from E. coli. Thus, this observation has far-reaching applications to the understanding of the interaction of the human host with many pathogens, not just TB.

Despite the global prevalence of the disease and its ancient association with the human population, current methods for the prevention, diagnosis and treatment of tuberculosis, especially its drug-resistant variants, remain inadequate. Through development of more sensitive detection techniques, earlier and more accurate diagnosis may become a simpler task.

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Authors: Rama Murthy Sakamuri, Dominique N. Price, Basil I. Swanson, Harshini Mukundan (all of Los Alamos National Laboratory), Myungsun Lee, Sang Nae Cho (International Tuberculosis Research Center, Changwon, Republic of Korea), Clifton E. Barry 3rd, Laura E. Via (Tuberculosis Research Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD)

Los Alamos National Laboratory

www.lanl.gov

(505) 667-7000

Los Alamos, NM

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